Amendments to the Claims/Listing of Claims

Please cancel claims 1-14 and 20-119 without prejudice and add new claims 120-141. This listing of claims will replace all prior versions, and listings, of claims in the application.

1-14 (Canceled)

15. (Original) A method for developing ligands with increased PIM specificity, comprising

testing a derivative of a kinase binding compound for increased PIM specificity, wherein increased specificity is indicative that said derivative is a ligand with increased PIM specificity.

16. (Original) The method of claim 15, wherein said kinase binding compound binds to at least 5 different human kinases.

17. (Original) The method of claim 15, wherein said kinase binding compound binds to at least 10 different human kinases.

18. (Original) The method of claim 15, wherein said PIM is PIM-1, PIM-2, PIM-3, or any combination of at least two of PIM-1, PIM-2, and PIM-3.

19. (Original) A method for identifying a ligand binding to PIM-1, comprising

determining whether a derivative compound that includes a core structure selected from the group consisting of Formula I, Formula II, and Formula III binds to PIM-1 with altered binding affinity or specificity or both as compared to the parent compound.

20-119 (Canceled)

120. (New) An in vitro method for obtaining improved ligands binding to PIM-1, comprising

determining whether a derivative of a compound that binds to PIM-1 and interacts with one or more of PIM-1 residues 49, 52, 65, 67, 121, 128, and 186 binds to PIM-1 with greater

affinity or greater specificity or both than said compound, wherein binding with greater affinity or greater specificity or both indicates that said derivative is an improved ligand.

121. (New) The method of claim 120, wherein said derivative has at least 10-fold greater affinity or specificity or both than said compound.

122. (New) The method of claim 120, wherein said derivative has at least 100-fold greater affinity or specificity or both.

123. (New) The method of claim 120, wherein said compound has a chemical structure of Formula I, Formula II, or Formula III.

124. (New) An in vitro method for developing ligands specific for PIM-1, comprising

determining whether a derivative of a compound that binds to a plurality of kinases has greater specificity for PIM-1 than said compound.

125. (New) The method of claim 124, wherein said compound binds to PIM-1 with an affinity at least 10-fold greater than for binding to any of said plurality of kinases.

126. (New) The method of claim 124, wherein said compound interacts with at least one of PIM-1 residues 49, 52, 65, 67, 121, 128, and 186.

127. (New) The method of claim 124, wherein said compound is a compound of Formula I, Formular II, or Formula III.

128. (New) The method of claim 124, wherein said compound binds weakly to said plurality of kinases.

129. (New) An in vitro method for developing ligands binding to PIM-1, comprising

identifying as molecular scaffolds one or more compounds that bind to a binding site of PIM-1;

determining the orientation of at least one molecular scaffold in co-crystals with PIM-1; and

identifying chemical structures of said molecular scaffolds, that, when modified, alter the binding affinity or binding specificity or both between the molecular scaffold and PIM-1; and

synthesizing a ligand wherein one or more of the chemical structures of the molecular scaffold is modified to provide a ligand that binds to PIM-1 with altered binding affinity or binding specificity or both.

130. (New) The method of claim 129, wherein said molecular scaffold is a weak binding compound.

131. (New) The method of claim 129, wherein said molecular scaffold binds to a plurality of kinases.

132. (New) The method of claim 129, wherein said molecular scaffold interacts with one or more of PIM-1 residues 49, 52, 65, 67, 121, 128, and 186.

133. (New) The method of claim 129, wherein said molecular scaffold has a chemical structure of Formula I, Formula II, or Formula III.

134. (New) An in vitro method for developing a ligand for a kinase comprising conserved residues matching one or more of PIM-1 residues 49, 52, 65, 67, 121, 128, and 186, comprising

determining whether a compound of Formula I, Formula II, or Formula III binds to said kinase.

135. (New) The method of claim 134, wherein said kinase comprises conserved residues matching at least 2 of PIM-1 residues 49, 52, 65, 67, 121, 128, and 186.

136. (New) The method of claim 134, wherein said kinase comprises conserved residues matching PIM-1 residues 49, 52, 65, 67, 121, 128, and 186.

137. (New) The method of claim 134, further comprising determining whether said compound modulates said kinase.

138. (New) The method of claim 134, wherein said determining comprises computer fitting said compound in a binding site of said kinase.

139. (New) The method of claim 134, further comprising forming a co-crystal of said kinase and said compound.

140. (New) The method of claim 139, further comprising determining the binding orientation of said compound with said kinase.

141. (New) The method of claim 134, wherein said kinase has at least 25% sequence identity to full-length PIM-1.